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# Criteria for Short-Term Exposures to Air Pollutants



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Committee on Toxicology

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Board on Toxicology and Environmental Health Hazards

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Assembly of Life Sciences

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CRITERIA FOR SHORT-TERM EXPOSURES  
TO AIR POLLUTANTS

COMMITTEE ON TOXICOLOGY

Board on Toxicology and Environmental Health Hazards  
Assembly of Life Sciences  
National Research Council

National Academy of Sciences  
Washington, DC

November 1979

## NOTICE

The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the Councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the Committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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## CRITERIA FOR SHORT-TERM EXPOSURES TO AIR POLLUTANTS

### INTRODUCTION

Since about 1969, the Environmental Protection Agency (EPA) and its predecessor, the National Air Pollution Control Administration (NAPCA), have published a number of criteria documents addressing the question of public exposure to a wide variety of air pollutants. National air-quality standards have been set for several of these. In most cases, a considerable body of information has been assembled to provide the best possible basis for recommendations for short-term and long-term exposures. The format of these documents has varied in detail, but has conformed to a general pattern: sources, occurrence, formation, disposal, and uses of the pollutants have been considered as background; effects on man and animals have formed the basis for determining permissible exposures; and effects on vegetation and materials and significant impact on ecology or the biosphere have been noted as potentially indicating the desirability of more stringent controls. During the same period, the National Institute for Occupational Safety and Health (NIOSH) has produced a number of criteria documents on substances encountered in the workplace. The National Research Council has contributed greatly to the literature on exposure to air pollutants through its Committee on Medical and Biologic Effects of Environmental Pollutants. In addition, the Committee on Toxicology has for several years been recommending short-term exposure limits for chemicals of concern to various federal agencies. Two sets of limits have been established by this Committee: occupational emergency exposure limits (EELs) for unpredictable exposures to military and space chemicals, and short-term public limits (STPLs) and public emergency limits (PELs) for predictable and unpredictable release, respectively, of various pollutants into the ambient air for short periods. Documents outlining the bases for establishing these exposure limits were published by the Committee in 1964<sup>9</sup> and 1971.<sup>10</sup>

Attitudes about acceptable exposure conditions for both occupational and general ambient air pollutants have changed substantially since the original guidelines were issued by the Committee on Toxicology in 1964, and the present Committee felt it was necessary to reassess and revise the criteria for short-term exposures to air pollutants. This document is the result of that effort. Previously, the Committee issued separate guidelines for military and space personnel and for the general public. The present Committee believes that a single set of criteria are sufficient for establishing short-term exposure limits for both the general public and more narrowly defined populations at risk, such as military or space personnel. For some of these population groups, such as a submarine crew, where the ranges of age and individual susceptibility are smaller than those among the general public, the Committee recognizes that there may be justification for different exposure limits for some substances.

### POLLUTANTS OF CONCERN

The following groups of air pollutants merit concern:

- General air pollutants: The focus of interest in the EPA has been on general air pollution, comprising airborne particles, sulfur and nitrogen compounds, oxidants, hydrocarbons, and carbon monoxide. These include the compounds for which

community standards have been set. The standards usually include short-term exposure limits.

• Specific compounds: A number of compounds are of great importance because of the potential long-term effects of prolonged exposure at low concentrations. These, however, are of less concern in this document, which focuses on short-term exposures.

• Other chemicals discharged by industry: The general public may be exposed to a wide range of chemicals whose presence results from industrial discharges. Many of these were reviewed by NAPCA.

• Chemicals used in the home: The general public is exposed to a large number of chemicals in and around the home, such as cleaning materials, floor and furniture polishes, cosmetics, pesticides, and materials that diffuse out of wood or plastic.

• Chemicals used in hospitals: Anesthetic gases and biologic aerosols can be cited as air pollutants of concern to the general public, as well as to those who work in hospitals.

• Chemicals for military and space application: Certain chemicals are of interest because of their potential for causing injury through the unpredictable exposure of military and space personnel.

#### DEFINITION OF SHORT-TERM EXPOSURE

For the purposes of this document, a short-term exposure is defined as a single exposure, usually lasting 60 min or less, but never more than 24 h. For evaluation of 24-h exposure limits, the variation in concentration over shorter periods may be an important consideration. In addition to length of exposure, it is important to differentiate between repeated exposures and exposures that are exceptional and may never be repeated. In the former cases, the frequency of occurrence and the time between exposures should also be noted.

#### FACTORS TO CONSIDER IN ESTABLISHING SHORT-TERM CONCENTRATIONS OF POLLUTANTS

Various types of evidence should be assessed in reaching a decision on permissible short-term exposures:

- Results of experimental exposures
  - (a) of humans
  - (b) of animals
- General observations on the effects of exposures of individual persons

- Epidemiologic observations on the development of disease and functional changes in groups of people (populations or segments of populations)
- Other factors:
  - (a) Nuisance effects
  - (b) Effects on vegetation and livestock
  - (c) Effects on materials
  - (d) Effects on the biosphere, ecology, etc.
- Long-term effects of short-term exposure, e.g., chronic hepatitis and cancer
- Interaction of factors

The most useful data on permissible short-term exposures come from observations on humans. Accidental high exposures, general observations on the effects of lower concentrations, epidemiologic observations on various populations groups, and planned experiments can provide a body of knowledge on dose-response (or exposure-effect) relationships from which it is possible to determine concentrations that are not likely to have adverse effects.

When human data are not available, recourse must be had to experimental exposures of various animals. Short-term effects on plants and materials should also be noted.

#### Experimental Exposures

##### Experimental exposures of humans

Human studies provide useful information on dose-response relationships for limited exposures to specific pollutants. They also may provide insight into the mechanism of effects. Data from inhalation exposures are probably most useful here, because of the direct relevance to the most likely route of exposure. Human experimentation is, however, seriously limited by ethical considerations to exposures that are readily tolerated and cause only reversible effects. It also may be limited to healthy persons in specific age ranges.

##### Experimental exposures of animals

Inhalation experiments with animals provide essential preliminary information about possible effects in man and the concentrations at which these effects may occur. They are useful in the identification of adaptations that may occur with repeated exposure. They enable hypotheses about the mechanism of action of pollutants to be tested. They offer a good opportunity to explore interactions between pollutants and other factors that may affect toxicity. Data from skin-absorption and ingestion studies are also useful and should be considered.

The extent to which animal experiments provide quantitative data on dose-response relationships that can be reliably extrapolated to humans is more debatable. Such data depend on the species used, and relevance to man is uncertain unless there is considerable information on the target organ and pharmacokinetics in both the animal and man. There are also uncertainties with respect to the similarities between chamber exposures and actual exposures, such as in the uniformity of the contaminated air mass and the possible deviations from the predicted movement of the air.

When data from animal testing are used to predict the effect of a substance on humans, a major uncertainty in the prediction is the extrapolation from a genetically homogeneous group of experimental animals to the genetically heterogeneous human population, which contains subpopulations with varied susceptibility. Given the present state of knowledge, we cannot be certain of the relationship between the biologic factors that determine the toxic effects in experimental animals and those which determine the effects in man.

#### General Observations from Human Exposures

General observations by the public and careful observations by the scientifically trained can be most valuable in the detection of functional changes that result from short exposures to pollutants. The concentrations involved in such exposures are usually uncertain or completely unknown. Consequently, these types of observations are more likely to provide only qualitative evidence on the effects of exposure. Sometimes, however, it is possible to obtain quantitative data. The National Air Surveillance Network and similar monitoring systems have provided at least crude estimates of the kinds of exposures to which people have been subjected. Exposures that occur in the occupational setting may be routinely monitored; and they may be much the same from day to day, so that monitoring is of value after the event. In these situations, exposure and response can be related in a quantitative way (e.g., in a dose-response curve).

#### Epidemiologic Observations

Whereas experimental exposures and general observations are primarily made on individuals, the focus of epidemiologic studies is on groups of people. The epidemiologist refers to these groups as populations or segments of populations, such as all persons living in a city, town, or other geographic area; all children in the first through third grades; whites; and blacks.

Many pollutants have had adverse effects on people's health first through transient air pollution episodes. If a system of monitoring is in operation, the effect of these exposures on people's health can be estimated. Thus, in the classical air pollution episodes, both excess mortality and morbidity were established early in the investigation. In London, episodes of exposure to smoke and sulfur dioxide, with each pollutant at a concentration in excess of about  $1 \text{ mg/m}^3$  of air, resulted in illness or death in susceptible individuals. This established a concentration that was considered unacceptable to the general public. Identification of a relatively safe concentration, however, required a great deal of work.

Most useful in this respect were the day-to-day monitoring of pollutant concentrations and the relating of these concentrations to day-to-day numbers of deaths and illnesses. Studies of this kind provided useful data both on the general population and on susceptible groups of bronchitic patients. They permitted the identification of a permissible concentration.

Other epidemiologic indexes may also be used to identify short-term effects, e.g., sickness and absence from school or work because of illnesses likely to be precipitated or exacerbated by air pollution, transient changes in lung or other organ functions, and development of symptoms or function impairment due to pollution.

#### Other Factors

As previously indicated there can be reasons other than health for controlling pollutants, although a potential health hazard usually receives the greatest weight.

#### Nuisance effects

Undesirable aesthetic effects, such as unpleasant odors and reduced visibility, and associated economic losses should be considered in connection with predictable exposures. They are not deemed to be important factors in developing standards for short-term unpredictable exposure.

#### Effects on vegetation and livestock

There are numerous examples of plant and animal sensitivity to air pollutants that do not appear to affect humans. Many plants are readily damaged by traces of ethylene, which have no effects on humans or animals. Grazing animals, especially sheep and cattle, are severely affected by airborne arsenic, lead, and molybdenum particles that are deposited on forage and then ingested. Instances of this type are sufficiently common to justify their consideration.

#### Effects on materials

In a few cases, brief releases of air pollutants have had substantial effects on materials, in addition to generally reversible effects on the health of exposed humans, plants, and animals. Gaseous sulfur compounds can cause discoloration of buildings painted with lead-based paints. Corrosive gases and vapors attack stone and metal; although the effect may not be immediately noticeable, these exposures can produce appreciable damage if sufficiently prolonged or repeated. The possibility of such effects should be taken into account.

#### Effects on ecology and biosphere

Examples of chemical air pollutants that have been regulated mainly because of their effects on ecologic systems and the biosphere are DDT and the fluorocarbons.

### Long-Term Effects of Short-Term Exposures

Although short-term adverse effects are of primary concern in the case of a single brief exposure, the development of chronic effects, such as liver or kidney disease or cancer, is a possibility for some substances. Data on the long-term health implications of brief exposure to chemicals are sorely lacking, and the Committee urges the development of appropriate test methods to obtain such data. The Committee recognizes the need, in the meantime, for the establishment of short-term exposure limits for many chemicals, whether or not long-term exposure to them is known or suspected to have irreversible effects. Because the magnitude of the problem varies, the possibility of long-term health effects must be judged substance by substance.

### Interaction of Factors

Exposures of the public to atmospheric pollutants seldom involves a single compound. The effects of any pollutant involved in a short-term episode may be modified by interaction with one or more additional pollutants. The interaction may be physical, as in absorption of gases on solid particles, or chemical, as in photochemical smog. It is therefore important to obtain information on the composition of air at the anticipated site of short-term exposure.

## CRITERIA USED TO ASSESS ACCEPTABLE EXPOSURE

### Mortality

Short exposure to a pollutant at high concentrations may result in death, which may be immediate or delayed. Mortality is a widely used and important index in animal experiments, and is also a most useful index of serious health effects in epidemiologic studies. Deaths from all causes and deaths from specific causes may be used; however, there can be inaccuracies in certifying causes of death.

Death rates may vary over time and from one place to another. Short-term variation in pollutant concentrations at different times of day, when related to variations in numbers of deaths, may provide valuable data on dose-response relationships. In assessing the concentration of a pollutant to which the public may safely be exposed, one needs to consider not only the healthy population (young, old, men, women, pregnant, physically active, exercising, etc.), but also persons with various diseases (such as asthma and emphysema), who may be particularly susceptible to the effects of pollutants.

### Morbidity (Illness)

Apart from killing people, pollutants may also make them ill. Many of the considerations that apply to mortality also apply to morbidity. Thus, illnesses

of all causes may be combined, or illnesses with specified causes may be considered separately. Unfortunately, it is usually much harder to obtain reliable information on morbidity than on mortality. Whereas statistics of mortality are usually available, much less information is available on morbidity and special surveys are often required.

Episodes of accidental exposure to exceptional concentrations of pollutants may provide valuable information on the effects of short-term exposure.

#### Physiological Measurements

##### Respiratory system

The main portal of entry of air pollutants is the respiratory tract. The development of respiratory symptoms, allergic sensitization, or changes in lung function provides evidence of the impact of pollutants. Of a large number of tests that can be used to measure changes in lung function, by far the most often used is spirometry. Widely used measures of the bellows function of the lung include the volume of air that can be expelled after a full inspiration (the forced vital capacity); the volume that can be expelled in a measured time, usually 1 s (the timed vital capacity or force expiratory volume in 1 s); and the ratio of the forced expiratory capacity to the forced vital capacity (expressed as a percentage). Less frequently used in assessing pollutants are airway resistance, dynamic compliance, gas-mixing, and uptake of blood gases from lung alveoli and their transfer to blood capillaries.

Evidence of change in the volume of mucus produced by the respiratory epithelial cells, mucous and serous glands, goblet cells, etc., can also provide information on the effects of exposure to pollutants.

Special tests to detect increased responsiveness of the respiratory passages to bronchoconstricting drugs have been used in connection with some pollutants.

Impairment of functional capacity under stress has sometimes been measured. For example, the effect of pollutants on athletic performance has provided evidence of impairment that might not have been detectable in normal activity.

##### Neuropsychologic tests

Some pollutants have effects on the central nervous system that are detectable in the lowest concentrations only by special psychologic tests. For the most part, these tests are designed to measure sensorimotor performance, e.g., fine discrimination, accuracy, and judgment.

##### Effects on the eye

Eye irritation and tearing have proved exceptionally valuable indicators of permissible exposures to some oxidants.

### Biochemical, enzyme, and immunologic changes

Additional evidence of an effect of pollutants on bodily function may be found in alterations in enzyme activity and biochemical and immunologic changes.

### Complaints

Complaints made by exposed individuals provide an important criterion on acceptability of pollutants. Although they may not necessarily be related to any health effects, they need to be considered as an indication of tolerable exposure.

### Measurement of Exposure

There are considerable difficulties in specifying the extent of an exposure. These start with measurement of the pollutant(s) of concern. Often, methods that have been in use for years are found to be inadequate. If adequate procedures are not available, the immediate need for research and development should be emphasized.

The physical form of a pollutant (gas, vapor, dust, or mist) may have a pronounced effect on the route and extent of its attack. Particles up to  $10\mu\text{m}$  in diameter can be inhaled into the lungs, whereas larger particles are filtered out in the upper respiratory passages. Such properties as solubility and chemical composition also alter the nature and degree of effect of a pollutant. Consequently, it is essential that the pollutant be well characterized.

There is often difficulty in estimating, from a fixed monitor, the extent of exposure of persons at some distance from the monitor. Short-term estimates of 24 h or less are also confounded by the fact that people spend some of their day at home, some at work, and some elsewhere and spend some of it indoors and some outdoors. Personal monitoring is one approach to obtaining an adequate integrated dose.

### CAUSE-AND-EFFECT RELATIONSHIPS AND ESTABLISHMENT OF EXPOSURE LIMITS

As far as is known, all living systems have some ability to withstand some injury from toxic chemicals. This resistance is due to mechanisms that modify absorption, metabolism, or excretion or that result in the development of adaptive cellular processes that may not be well characterized. Whenever the capacity of these protective mechanisms is exceeded by the effects of the toxicants, there is damage, which should be observable by measuring an appropriate characteristic like those discussed above. Beyond the threshold at which there is no observable biologically important effect from a given dose, the extent of the effect, i.e., the degree of injury, will increase with increasing dose of toxicant, with death of the organism as the upper limit. Two concepts are involved here, threshold and dose-response, which are accepted as applying to the actions of most substances. In special

cases, both concepts may be inapplicable. The relationship between dose and response is known with certainty only in the range of experimental observation. Estimation of the response at doses beyond the range of experimental data requires extrapolation. Although several statistical procedures have been developed and applied for this purpose, none has an adequate biologic basis; therefore, considerable uncertainty may be associated with results obtained by application of these procedures.

In practice, there may be a serious problem in identifying a "biologically important effect," since this effect is determined by the test used, and the most appropriate test may not be known.

#### Acquisition of Human Data

In establishing exposure limits for chemicals, use of reliable dose-response data from human exposure is the method of choice, and such data should be obtained and used whenever possible. However, human data are generally limited to accidental exposure to high concentrations of chemicals and experimental, general, and epidemiologic observations. Accidental exposure and general observations often do not provide sufficient quantitative data to examine dose-response relationships. Epidemiologic data can be limited by the amount of information available on the extent of exposure. In addition, few epidemiologic studies are available on effects of short-term exposure to chemicals. Human experimentation can provide important information on dose-response relationships, but is obviously limited by ethical considerations.

When applying human data obtained from individuals or specific population groups to the general population, one must take into account the variations in genetic and health state among humans that may affect their susceptibility to air pollutants. Examples of effects of genetic variations are allergic asthma, familial pulmonary emphysema and serum antitrypsin deficiency, susceptibility to lead poisoning and deficiency of the enzyme glucose-6-phosphate dehydrogenase in the red blood cells, male susceptibility to chronic granulomatous disease and leukocyte deficiency of glucose-6-phosphate dehydrogenase, and sickle-cell anemia and enhanced risk of effects of carbon monoxide. Application of safety factors and statistical estimates of risk can be used to take into account the range of human susceptibilities and are discussed in further detail below.

#### Acquisition of Data by Animal Experiment

The data necessary to evaluate the relationship between exposure to a pollutant and its effects on the population at risk are not always available from human experiences. For many air pollutants, further study in animals will be needed, and the data should be derived from at least two species. The data are presented in relation to human health concerns, but the principles involved apply to other concerns.

### Data from animal experiments

Animal data should include:

- The most sensitive target organ(s) or body system(s) affected by short-term exposure to the air contaminant in question.
- Adequate characterization of the nature of the effect on the target(s).
- The range of the dose-response relationship for the target(s), from no effect to severe effects.
- The rate of recovery from reversible effects.
- The nature and severity of injury at which the effect ceases to be reversible.
- Identification of cumulative effects, if any, such as cancer.
- Identification of pharmacokinetic data and comparison with data obtained on humans.
- The effects of interaction, if any, of the toxicant with other air pollutants and the concentrations at which the interaction occurs.
- Identification of types of functional abnormalities and pathologic states that may also exist among the potentially exposed human population and may render them more susceptible to the pollutant.

### Interpretation of the data

Interpretation of the information derived from animal experiments requires experienced scientific judgment in a variety of disciplines. The evaluation should consider the conditions under which the data were obtained and, in particular, their relevance to the conditions of human exposure. How similar are the test species and the test organ in morphology, in sensitivity of response to the pollutant, and in metabolism and disposition of the pollutant to man and the corresponding human organ? Were the observed animal responses the consequences of exposure conditions to which the public may be subjected?

### Translation of animal data to humans

Development of short-term exposure limits requires that animal data be translated in a quantitative way to the human response. The response of the species most representative of man, considering both toxicologic and pharmacokinetic characteristics, should be used for determination of the appropriate exposure limit. If data are not available on which species best represents man, it is prudent to use data from the most sensitive animal model to set appropriate limits. It should be noted that the use of data from animal experiments and in vitro tests may yield values

surrounded by considerable uncertainty.

Safety factors have had considerable use in the past when an estimate of the maximum no-observed-adverse-effect dose was available. The preferred term now is an uncertainty factor, which represents the level of confidence that is justified on the basis of the animal and human toxicity data.<sup>11</sup> In the absence of maximum no-observed-adverse-effect doses, one must resort to other methods of estimating risk. More recently, methods devised for evaluating risk from carcinogens have been applied to other toxic substances.

In the application of uncertainty factors, an estimate can be made on the basis of the lower range of the most susceptible humans. Those at unusual risk may include persons at either extreme of age, of particular nutritional state, with preexisting disease, with hereditary susceptibility, or even at greater risk because of unusual physical exertion. All these factors, and standardized calculations based on extrapolation from experimental animals to man using surface area and body weight, can be used.<sup>13</sup> The drawback of the uncertainty-factor method is that the factor usually must be chosen without recourse to precise data on most of the above estimates of susceptibility. Values 100-fold below the no-observed-adverse-effect level in lifetime animal experiments have sometimes served as the basis for calculation of acceptable daily intake (ADI) of chemicals. Larger uncertainty factors have sometimes been used. For example, a 1,000-fold factor is usually used to calculate the ADI for food additives when 90-day rodent studies are the basis. Higher uncertainty factors may also be used, depending on the quality of the lifetime studies.

Attempts to estimate risks on a precise quantitative basis have resulted from the pioneering work of Mantel and Bryan<sup>8</sup> in carcinogenesis. The original work has been reviewed by several authors.<sup>2,3,7</sup> The Mantel-Bryan procedure used a probit model to extrapolate from an upper bound on observed dose-response data to estimate the dose corresponding to a specified degree of risk (e.g., 1 in 1 million) or to estimate the risk at a specified dose below the experimental range. The certainty of the estimated dose (or the risk corresponding to a specified dose) is unknown, but, because an upper bound (e.g., 99% confidence limit) is used, the estimate is likely to be conservative.

Other statistical models have been proposed - such as linear extrapolation and curvilinear extrapolation - to estimate the risk of delayed, irreversible toxic effects.<sup>6</sup> These, as well as the probit model, require the imposition of assumptions that contribute to uncertainty. But they do have an advantage over the use of uncertainty factors, in that they can be applied in the absence of no-observed-adverse-effect data.

New methods of estimating risk are being developed, and this field may change in the near future.

### Establishing Exposure Limits

The approach to establishing short-term exposure levels is judged on a substance-by-substance basis. For many compounds, such as upper respiratory tract irritants, where there is reliable human data, the animal data are sound, and the degree of confidence is high that irreversible effects from a single exposure will not occur, then the Committee might establish exposure limits directly from the available data. For compounds where there are little human data, but the animal data are sound and it is unlikely that irreversible effects will occur from a single exposure, an uncertainty factor might be employed, the magnitude of which will depend on the quality of the data. When the evidence suggests that cancer or some other irreversible effect may occur, the Committee may choose to provide an estimate of the level of risk of the effect occurring rather than recommend an exposure limit. However, given the fact that the concern in this document is for single, short-term exposures, the Committee has concluded that, for compounds in the latter case, several other approaches are also available to them. These include recommending an exposure limit using an appropriate uncertainty factor as in the approach for noncarcinogens, recommending an exposure limit along with a risk estimate for the possible irreversible effect, or recommending an exposure limit along with cautionary statements to protect particular segments of the population when they are known to be at increased risk, such as when the data suggest possible teratogenic effects.

### SELECTION OF STANDARDS: SHORT-TERM PUBLIC LIMITS (STPLs), SHORT-TERM PUBLIC EMERGENCY LIMITS (SPELs), AND EMERGENCY EXPOSURE LIMITS (EELs)

#### Definitions

SHORT-TERM PUBLIC LIMITS (STPLs) are those which relate to predictable single exposures, usually lasting 60 min or less, but never more than 24 h. STPLs are limits that, if not exceeded, are expected to be associated with only a remote possibility of a nonincapacitating, reversible effect in an exposed population. They differ from air-quality standards in that the STPLs are intended for infrequent exposures. A nonincapacitating, reversible effect is one that will not cause a period of disability; will not impair one's vision, visibility, judgment, or ability to breathe; and will not interfere with one's ability to escape from the site of the exposure.

SHORT-TERM PUBLIC EMERGENCY LIMITS (SPELs)\* are those which relate to unpredictable single exposures, usually lasting 60 min or less, but never more than 24 h, and whose occurrence is expected to be rare in the lifetime of any one individual. SPELs reflect an acceptance of the statistical likelihood of the occurrence of a nonincapacitating, reversible effect in an exposed population. They are designed to avoid significant decrements in performance during emergencies and might contain no uncertainty factor. The acceptable level of risk will depend on the specific compound in question and the type of effect produced by the compound. SPELs are concentrations acceptable to the public in emergencies, such as civil defense or defense of neighborhood property in the case of fire.

\*It should be noted that the Committee originally designated exposure limits for unpredictable single exposures of the general public as public emergency limits (PELs). However, in order to avoid possible confusion with the Occupational Safety and Health Administration (OSHA) permissible exposure limits, the Committee renamed the PELs and now refers to them as short-term public emergency limits or SPELs.

EMERGENCY EXPOSURE LIMITS (EELs) differ from SPELs only in that they apply to defined occupational groups, such as military or space personnel, rather than the general public. Because the relevant populations at risk are more narrowly defined than the general public and are generally younger and healthier, an EEL for a specific chemical may differ quantitatively from the SPEL for the same substance. These values will depend on the available data and the collective judgment of the committee recommending the exposure limits.

#### Balance of Risks

Of all the risks associated with the release of a pollutant, the concentration that carries the least risk to health is selected as the upper limit for the concentration of the pollutant for a short-term exposure. This selection involves study of the biologic effects of the pollutant, its source, and the reasons for its presence.

Studies may be needed to permit the responsible government agency to relate the health risk of short-term exposure to the alternative risks that might attend abandonment of the operation or the application of various degrees of control. An example is the firing of a rocket during research, development, training, or launch by a federal agency, such as the National Aeronautics and Space Administration or the Department of Defense. When the risks have been evaluated, the agency can provide the appropriate options to reduce the risks to the public to an acceptable point by setting short-term limits for predictable exposures (STPLs).

An example involving the private sector is the testing of a new firefighting technique or the training of firemen. The extent of public exposure to smoke and to the firefighting agent and its pyrolysis products is predictable. Among the risks to be evaluated and balanced would be the risk of health and other effects, which are the subject of these guides, and the risk to the public of the absence of adequate fire protection.

Associated with both the foregoing examples is another risk: the possibility of the accidental release of the rocket fuels or firefighting agents as the result of a spill. These would be unpredictable exposures and would be the subject of SPELs and EELs.

#### Acceptable Risks

A risk to health must be appraised from the view of establishing what, if any, is an acceptable effect. Two of the important factors to be considered are the duration and frequency of an exposure. Severe or permanent disability cannot be tolerated. Even a minor effect, such as a mildly unpleasant odor or slight irritation of the eyes and nose, if it occurs frequently, can become sufficiently objectionable to be considered in the selection of a short-term exposure limit.

The evaluation of the risks associated with unpredictable exposure requires consideration of the probability of an accident. Such risks can never be eliminated, but they can be minimized by proper planning of operations and equipment design. Exposure to an accidentally released air pollutant should be a rare event in the lifetime of an individual. However, because of the nature of such an event, some risk of reversible effects from exposure to the pollutant may be judged to be acceptable.

#### Comparison with Other Exposure Limits

Several government and nongovernment organizations recommend different exposure limits for air pollutants, which can lead to confusion in attempts to apply them.

The American Conference of Governmental Industrial Hygienists (ACGIH) annually recommends Threshold Limit Values (TLVs) for substances in workroom air. The TLVs, as defined in ACGIH's most recent publication<sup>1</sup> on the subject, fall into three categories:

- Threshold limit value-time weighted average (TLV-TWA): the time-weighted average concentration for a normal 8-h workday or 40-h workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect.
- Threshold limit value-short term exposure limit (TLV-STEL): the maximal concentration to which workers can be continuously exposed for a period up to 15 min without suffering irritation, chronic or irreversible tissue change, or narcosis of sufficient degree to increase accident proneness, impair self-rescue, or materially reduce work efficiency, provided that no more than four excursions per day are permitted, with at least 60 min between exposure periods, and provided that the daily TLV-TWA also is not exceeded. The STEL should be considered a maximum allowable concentration, or ceiling, not to be exceeded at any time during the 15-min excursion period. ACGIH notes that the STEL should not be used as an engineering design criterion or considered as an emergency exposure limit (EEL).
- Threshold limit value-ceiling (TLV-C): the concentration of a material that should not be exceeded even instantaneously.

The Occupational Safety and Health Administration (OSHA) in 1971 adopted the 1968 TLVs and certain standards issued by the American National Standards Institute (ANSI Z-37 series) as the official federal standards for air contaminants in industrial air.<sup>5</sup> OSHA has since promulgated new permissible exposure limits for some of these contaminants, but has retained the ACGIH and ANSI recommendations for most.

The National Institute for Occupational Safety and Health (NIOSH) also recommends occupational exposure limits through the publication of criteria documents. These limits, which do not become federal standards until adopted by OSHA, are generally either time-weighted averages for a 10-h workday and 40-h workshift or ceiling concentrations for specified sampling periods.

The Pennsylvania Department of Health has recommended short-term limits for exposure to various air contaminants for specified brief periods.<sup>12</sup> It states that the concentration represents an upper limit of exposure for the specified time and assumes that there are sufficient periods between episodes for recuperation. The daily average exposure to the contaminant, including these episodes, shall be such that the threshold limit value shall not be exceeded.

The Environmental Protection Agency (EPA) has promulgated national ambient air quality standards for six criteria pollutants, which are generally based on annual exposure to the pollutant.<sup>4</sup>

Exposure limits recommended by the Committee on Toxicology differ in their intent from those mentioned above. The Committee limits apply to rare or infrequent exposures of short duration and are not applicable to the routine exposure situations encountered in industrial settings or in the ambient air. The other limits previously described assume long-term exposure to the chemicals, whether in workroom or ambient air, under normal circumstances. Even the ACGIH TLV-STELs and the Pennsylvania short-term limits are set within the context of an 8-h/d, 40-h/wk exposure. In addition, because the EELs are established for narrowly defined populations, they should not be used as guidelines for all occupational groups. The Committee limits are designed to be of help in planning-e.g., to assist in advance preparations for emergencies in which chemicals are released to the atmosphere, to assist in establishing procedures for handling and using chemicals, and to assist in site selection for installations with regard to their proximity to residential areas.

#### REFERENCES

1. American Conference of Governmental Industrial Hygienists. 1978. Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1978. Cincinnati, OH.
2. Brown, C.C. 1976. Mathematical aspects of dose-response studies in carcinogenesis-the concept of thresholds. *Oncology* 33:62-65.
3. Cornfield, J. 1977. Carcinogenic risk assessment. *Science* 198: 693-699.
4. Environmental Protection Agency. 1977. National Primary and Secondary Ambient Air Quality Standards. 40 CFR 50.
5. Fed. Regist. 36:10504. May 29, 1971.
6. Hoel, D.G., Gaylor, D.W., Kirschstein, R.L., Saffiotti, U., and Schneiderman, M.A. 1975. Estimation of risks of irreversible, delayed toxicity. *J. Toxicol. Environ. Health* 1:133-151.
7. Mantel, N., Bohidar, N.R., Brown, C.C., Ciminera, J.L., and Tukey, J.W. 1975. An improved Mantel-Bryan procedure for "safety" testing of carcinogens. *Cancer Res.* 35:865-872.
8. Mantel, N. and Bryan, W.R. 1961. "Safety" testing of carcinogenic agents. *J. Natl. Cancer Inst.* 27:455-470.
9. National Research Council, Committee on Toxicology. 1964. Basis for Establishing Emergency Inhalation Exposure Limits Applicable to Military and Space Chemicals. Washington, D.C.: National Academy of Sciences.
10. National Research Council, Committee on Toxicology. 1971. Basis for Establishing Guides for Short-Term Exposures of the Public to Air Pollutants. Washington, D.C.: National Academy of Sciences.
11. National Research Council, Safe Drinking Water Committee. 1977. Drinking Water and Health. Washington, D.C.: National Academy of Sciences.
12. Pennsylvania Department of Health, Division of Occupational Health. 1969. Supplement #1 to Short-Term Limits for Exposure to Airborne Contaminants: A Documentation, 1967-1969. Harrisburg, PA.
13. World Health Organization. 1967. Procedures for Investigating Intentional and Unintentional Food Additives. WHO Technical Report Series No. 348. Geneva.